IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	:	Examiner: Anne Marie Sabrina Wehbe
JEFFRIES, William Arthur et al.	)	
	:	Group Art Unit: 1633
Application No.: 10/046,542	)	
	:	
Filed: January 16, 2002	)	
	:	
For: METHOD OF ENHANCING AN IMMUNE RESPONSE	)	
	:	

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TERMINAL DISCLAIMER

Sir:

Petitioner, The University of British Columbia, having its principal place of business at University-Industry Liaison Office, #103, 6190 Agronomy Road, Vancouver, British Columbia, V6T 1Z3, CANADA, represents that it is the owner of the entire right, title, and interest in and to U.S. Patent Application Serial No. 10/046,542, filed 01/16/2002, which is a continuation-in-part of U.S.. Patent Application No. 08/817,731, filed 07/21/1997 (now U.S. Pat. No. 6,361,770), which is a continuation-in-part of U.S. Patent Application No. 08/311,442, filed 09/23/1994 (now abandoned), by virtue of an Assignment filed and recorded on 03/16/2005, on Reel/Frame 015905/0313, in the United States Patent and Trademark Office.

Petitioner, University of British Columbia, hereby disclaims the terminal part of the term of any patent granted on the above identified patent application which would extend beyond the full statutory term, as shortened by any terminal disclaimer, of U.S. Patent 6,361,770, and hereby agrees that any patent so granted on the above identified patent application shall be enforceable

only for and during such period that the legal title to U.S. Patent 6,361,770 shall be the same as the legal title to any patent granted on the above identified patent application, this agreement to run with any patent granted on the above identified patent application and to be binding upon the grantee, its successors or assigns.

In making the above disclaimer, Petitioner does not disclaim any terminal part of any patent granted on the above identified patent application, prior to the full statutory term of U.S. Patent 6,361,770 as defined in 35 U.S.C. §§154-156 and 173, in the event that U.S. Patent 6,316,770 expires for failure to pay a maintenance fee, is held unenforceable or is found invalid in a final judgment by a court of competent jurisdiction, is statutorily disclaimed in whole or terminally disclaimed under 37 CFR §1.321(a), has all claims cancelled by a re-examination certificate or as a result of an interference proceeding, or is otherwise not deemed to provide the rights conveyed by 35 USC §154, prior to the full statutory term of U.S. Patent 6,316,770 as defined in 35 USC §§154-156 and 173, except for the separation of legal title stated above.

Further, Petitioner does not disclaim any terminal part of a patent granted on the above identified patent application that would extend beyond the present termination of U.S. Patent 6,316,770, in the event that such present term is extended by virtue of compliance with the conditions for term extension of any present or future patent term extension provisions of the patent law, including but not limited to 35 U.S.C. §§155,155A or 156, and without waiving Petitioner's right to extend the term of a patent granted on the above identified patent application to the extent provided by law.

The undersigned, being the Attorney of Record for the above identified patent application, and duly authorized to act on behalf of Petitioner, certifies that he has reviewed the Assignments as mentioned above, and to the best of his knowledge and belief, legal title to the above identified patent application and U.S. Patent 6,361,770 rests with Petitioners, University of British Columbia. The undersigned declares that all statements made herein of his own knowledge and true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that wilful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001, Title

18 of the United States Code, and that such wilful false statements may jeopardize the validity of the above-identified application or any patent issuing therefrom.

Respectfully submitted,

Date: January 18, 2007

By: 

LANG MICHENER LLP
Customer No. 35222
Telephone: (416) 307-4161
Facsimile: (416) 304-3868

ORIN DEL VECCHIO
Attorney for Applicant
Registration No. 57777

Atty Dkt: 50500-963 PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Commissioner for Patents
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Alexandria, VA 22313-1450

REQUEST FOR CONTINUED EXAMINATION AND PETITION FOR EXTENSION OF TIME

Sir:

The present letter is filed in response to the final office action dated July 13, 2005 and the Notice of Appeal dated January 12, 2006. Applicant is simultaneously filing a Request for Continued Examination (RCE) and a Request for a two-month extension of time.

In response to the July 13, 2005 Final Office Action, please enter the following amendments and remarks.

Amendments to the Claims are reflected in the listing of claims which begins on page 3 of this paper.

Remarks begin on page 6 of this paper.

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently Amended) A method of enhancing an immune response to ~~an~~ a viral antigen comprising administering an effective amount of an agent that can augment the level of a ~~TAP~~ TAP-1 molecule or a TAP-2 molecule in a target cell bearing the viral antigen to a cell or animal in need thereof,

wherein the agent is a ~~nucleic acid sequence~~ vector comprising a nucleic acid sequence encoding ~~a TAP~~ the TAP-1 molecule or the TAP-2 molecule; and

wherein the vector is capable of transforming the target cell so that the expression of TAP-1 or TAP-2 is increased and the immune response to the viral antigen is enhanced ~~administration of the agent enhances the immune response to the antigen~~.

2. (Canceled)

3. (Original) A method according to claim 1 wherein the target cell is a virally infected cell.

4. (Canceled)

5. (Canceled)

6. (Canceled)

7. (Previously presented) A method according to claim 1 further comprising administering a nucleic acid sequence encoding an antigen.

8. (Original) A method according to claim 7 wherein the antigen is a viral antigen.

9. (Canceled)

10. (Canceled)

11. (Canceled)

12. (Canceled)

13. (Canceled)

14. (Original) A method according to claim 1 wherein the agent is administered intraperitoneally, subcutaneously, intravenously, orally, mucosally, submucosally or intradermally.

15. (Canceled)

16. (Cancelled)

17. (Currently amended) A method according to claim ~~16~~1 wherein the vector is a viral vector.

18. (Original) A method according to claim 17 wherein the viral vector is selected from the group consisting of vaccinia based vectors, adenovirus based vectors, lenti virus based vectors and HSV based vectors.

19. (Currently amended) A method according to claim ~~16~~1 wherein the vector is a plasmid.

20. (Previously presented) A method according to claim 19 wherein the plasmid is in a liposome formulation.

21. (New) A method of enhancing an immune response to an a tumor antigen comprising administering an effective amount of an agent that can augment the level of a TAP-1 molecule in a target cell bearing the tumor antigen to a cell or animal in need thereof,

wherein the agent is a vector comprising a nucleic acid sequence encoding the TAP-1 molecule; and

wherein the vector is capable of transforming the target cell so that the expression of TAP-1 is increased and the immune response to the tumor antigen is enhanced.

22. (New) The method according to claim 21, wherein the target cell is a tumor cell.

23. (New) The method according to claim 21, further comprising administering a nucleic acid sequence encoding an antigen.

24. (New) The method according to claim 23, wherein the antigen is a tumor antigen.

25. (New) The method according to claim 21, wherein the animal is also subjected to surgery, radiation, chemotherapy, immunotherapy or photodynamic therapy.

26. (New) The method according to claim 21, wherein the agent is administered intraperitoneally, intratumorally,

subcutaneously, intravenously, orally, mucosally, submucosally or intradermally.

27. (New) The method according to claim 21 wherein the vector is a viral vector.

28. (New) The method according to claim 27 wherein the viral vector is selected from the group consisting of vaccinia based vectors, adenovirus based vectors, lenti virus based vectors and HSV based vectors.

29. (New) The method according to claim 21 wherein the vector is a plasmid.

30. (New) The method according to claim 29 wherein the plasmid is in a liposome formulation.

REMARKS/ARGUMENTS

By the present amendment, claims 1, 17 and 19 have been amended, claims 4-6, 9-12 and 16 have been cancelled, and new claims 21-30 have been added. Claims 1, 3, 7-8, 14, and 17-30 are currently pending in the application. The amendments to the claims have been made without prejudice and without acquiescing to any of the Examiner's objections. Applicants reserve the right to pursue any of the deleted subject matter in a further divisional, continuation or continuation-in-part application.

The amendment does not contain new matter and its entry is respectfully requested.

The Official Action dated July 13, 2005 has been carefully considered. It is believed that the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

35 USC 112, first paragraph (Enablement)

The Examiner has rejected claims 1, 3-12 and 14-20 under 35 USC 112, first paragraph, for lack of enablement.

Type of Antigen

The Examiner has rejected the claims alleging that there is lack of enablement of enhancing an immune response to any antigen. In order to facilitate allowance, Applicant has amended claim 1 to a method of enhancing an immune response to a viral antigen. In addition, Applicant has added new claims 21-30, which are directed at methods of enhancing an immune response to a tumor antigen. Applicant respectfully submits that the claims as amended are enabled. For instance, Examples 8, 12, 18 and 19 provide support for viral antigens, and Examples 9-11, 13, 17 and 20-22 provide support for tumor antigens.

TAP-1 or TAP-2

The Examiner has rejected the claims for lack of enablement, alleging that a skilled artisan would not consider the transfection of either TAP-1 or TAP-2 alone into cells expressing little to no TAP-1 and TAP-2 as sufficient to enhance or increase presentation of endogenous peptide/MHC class I on the cell surface.

In response, Applicant has amended the claims and provides the following arguments. Specifically, claim 1 was amended to be directed to a method of enhancing an immune response to a viral antigen by enhancing the level of TAP-1 or TAP-2 in a cell. In addition, new claims 21-30 were added, and are directed to methods of enhancing an immune response to a tumor antigen by enhancing the level of TAP-1 in a cell.

Viral Experiments

The Examiner has stated that the Examples show that of 3 viral antigens tested, antigens derived from HSV are TAP independent, such that TAP expression did not enhance immune responses; immune response to antigens derived from Influenza virus require the expression of both TAP1 and TAP2; and only immune responses

to antigens from VSV can be enhanced by the expression of TAP1 alone.

Applicant concurs with the Examiner's finding that cells transfected with TAP-1 alone are able to present VSV antigens for an enhanced immune response as compared to non-transfected cells. Applicant respectfully submits that the VSV experiments (see Example 12) also support an enhanced immune response when the cells are transfected with TAP-2 alone. The Examiner noted that TAP-2 transfected cells showed approximately half the amount of specific lysis of the TAP-1 transfected cells. However, even though TAP-1 alone enhanced the CTL response better than TAP-2 alone, TAP-2 alone still enhanced the CTL response as compared to the untransfected cells (no TAP-1 or TAP-2 expression). Please see Example 12, Figure 14. Thus, the transfection of either TAP-1 alone or TAP-2 alone into cells was able to enhance VSV antigen presentation for an enhanced CTL response.

The Examiner has also stated that the examples show that transfection of TAP-1 alone is not sufficient to allow processing and presentation of endogenous Influenza peptides. Applicant attaches a Declaration of inventor Dr. Jefferies, which was submitted during prosecution of the patent application

United States Application no. 08/817,731. The Declaration describes experiments where CMT cells were transfected with TAP-1 (CMTr1) or TAP-2 (CMTr2). The results show that both CMTr1 and CMTr2 can present Influenza A antigens to CTLs, while the TAP deficient line CMT.64 can not. Please see Figure 3, which is attached as Exhibit E of the Declaration.

Figure 18 of the application as filed shows the results of experiments done with Influenza. Applicant respectfully points out that for each of the E:T ratios of 12.5, 25 and 50 there is an enhanced CTL response against Influenza antigens for the CMT cells expressing TAP-1 alone (CMTr1.4) as compared to the untransfected CMT cells, which are TAP-1 and TAP-2 deficient. There is greater enhancement of the CTL response seen using the CMT cells that express both TAP-1 and TAP-2 (CMTr12.12) as compared to the CMT cells expressing TAP-1 alone (CMTr1.4). However, this is likely due to the dose of Influenza used for these experiments, because the CTL response is dose dependent.

Further, the Examiner has stated that the examples show that neither TAP-1 nor TAP-2 is needed to enhance antigen presentation of cells infected with HSV. As reported in the attached article by Ahn, K. et al. (EMBO; 1996; 15(13): 3247), HSV has evolved a unique mechanism to evade the immune response.

Specifically, HSV expresses ICP47, which is a protein that inhibits TAP-mediated translocation of antigen-derived peptides across the endoplasmic reticulum. This prevents assembly of peptides with class I MHC molecules in the ER and ultimately recognition of HSV-infected cells by cytotoxic T-lymphocytes. The results of Figure 19 of the application as filed reflect this ability of HSV to evade the immune response.

In summary, Applicant has shown that either TAP-1 alone or TAP-2 alone can enhance the immune response to viral antigens. Accordingly, the Applicants respectfully submit that claim 1 and the dependent claims thereon are supported by the application.

Tumor Experiments

The Examiner has stated that the Examples do not support the transfection with TAP-2 alone to increase an anti-tumor CTL response. Specifically, the Examiner has stated that the examples show that the transfection with TAP-2 alone is not as effective to enhance a tumor specific CTL response as compared with TAP-1 alone. The Examiner has directed Applicant to Examples 21 and 22, particularly page 74.

In order to facilitate allowance, Applicant has amended claim 1 to remove reference to tumor antigens, and have added new claims

21-30. The new claims are directed to methods of enhancing an immune response to a tumor antigen by enhancing the level of TAP-1 in a cell.

In light of the above, the Applicants respectfully submit that claims 21-30 are fully enabled by the application.

Administration

The Examiner has stated that there is lack of enablement for other types of plasmid or viral vectors *in vivo*, other than recombinant vaccinia virus. In addition, the Examiner has stated there is lack of enablement for other routes of delivery of TAP into tumor cells, other than delivery to the site of the tumor. Further, the Examiner has stated that there is no guidance in the specification concerning dosages and routes of *in vivo* delivery for any and all vectors which encode TAP. Applicant respectfully traverses these objections for the following reasons.

The use of recombinant vaccinia virus is one example of how a gene encoding TAP can be introduced into a cell. A person skilled in the art will appreciate that other plasmids or viral vectors can be used. For example, please see the attached article by Dr. Jefferies (Lou, Y *et al.*, Cancer Res 2005;

65(17): 7926), which provides another example of how to express TAP in a cell. In these experiments, a nonreplicating adenovirus expressing human TAP1 was used to restore the expression of TAP1 in CMT.64 cells. Thus, Applicant respectfully submits that the application is enabled for other types of plasmid or viral vectors.

Applicant has additionally enclosed an April 26, 2001 publication in Nature by Shankaran et al. for the Examiner's review. This group administered TAP-1 intraperitoneally (i.p.) and showed that by this route of delivery mouse survival was increased. In this regard, we refer to page 519 "Contribution of TAP-1 to Cancer Therapy" and the Experimental Protocol section entitled "Generation of Effector Cell Populations" on page 520. As a result, Applicant has enabled both systemic as well as intratumoral administration of TAP molecules.

Applicant would also like to direct the Examiner to page 5, paragraph 64 and page 9, paragraphs 106-108 of the application as published. A person skilled in the art will appreciate, as described in the specification, that the dosage and routes of *in vivo* delivery can be adjusted to provide optimum therapeutic response. For example, the dosage may vary according to disease state, age, sex and weight. Further, dosage may depend on the

route of delivery. Optimal dosages and routes of delivery can be determined by trial that does not require undue experimentation.

In light of the above, the Applicants submit that the pending claims are fully supported by the application.

Genes Inducible by Tapasin

The Examiner has stated that there is lack of enablement for genes inducible by tapasin.

In order to facilitate prosecution, the Applicants have deleted claims 10 and 11 without prejudice.

In light of the above, the Applicants respectfully request that the rejection to claims 1, 3-12 and 14-20 pursuant to 35 U.S.C. 112, first paragraph for lack of enablement be withdrawn.

35 USC 112, first paragraph (Written Description)

The Examiner has rejected claim 10 pursuant to 35 U.S.C. 112, first paragraph, as lacking adequate written description for any gene which is inducible by tapasin.

As stated above, in order to facilitate prosecution the Applicants have deleted claims 10 and 11.

In light of the above, the Applicants respectfully request that the rejection to claim 10 as lacking written description pursuant to 35 U.S.C., first paragraph, be withdrawn.

35 U.S.C. 102

Spies et al. (1992)

The Examiner has rejected claims 1-5, 7-8, 16 and 19 under 35 U.S.C. 102(b) as being anticipated by Spies et al. (1992) Nature, Vol. 355, 644-646. Specifically, the Examiner has stated that Spies et al. teaches enhancement of CTL response against an LCL mutant .134, in which the TAP-1 gene is missing, but TAP-2 is present, following the co-administration of a vaccinia virus encoding a viral antigen and plasmid vector encoding TAP-1 to the cells *in vitro*. Applicant respectfully traverses this objection for the reasons given below.

Powis et al. (1991)

The Examiner has rejected claims 1-4, 6-8, 16 and 19 under 35 U.S.C. 102(b) as being anticipated by Powis et al. (1992) Nature, Vol. 354, 528-531. Specifically, the Examiner has stated that Powis et al. teaches the enhancement of CTL response

against a mutant tumor cell RMA-S, which lacks functional expression of TAP-2, following the co-administration of influenza virus, which encodes influenza viral antigens and a plasmid vector encoding TAP-2 to the cells *in vitro*. Applicant respectfully traverses this objection for the reasons given below.

Applicant respectfully submits that the present inventors have shown that TAP-1 alone or TAP-2 alone is able to enhance the processing and presentation of viral antigens. The prior art cited by the Examiner teaches that both TAP-1 and TAP-2 are required for peptide transport of viral antigens.

Applicant notes that Spies et al. used a mutant .134 cell which is missing the TAP-1 gene, but has the TAP-2 gene, and that Powis et al. used a mutant RMA-S cell, which is missing functional expression of TAP-2, but expresses TAP-1. These two references teach that both TAP-1 and TAP-2 are needed in order for viral antigen processing and presentation. In contrast, Applicant has data to show that either TAP-1 alone or TAP-2 alone can augment an immune response to viral antigens. For instance, Applicant has used CMT.64 cells which are defective in both TAP-1 and TAP-2, and have shown that augmenting the expression of either TAP-1 alone or TAP-2 alone can enhance the

presentation of viral antigens (See Examples 8-12 of the application).

In light of the above, the Applicants respectfully request that the rejection to the claims as anticipated by Spies *et al.* or Powis *et al.* be withdrawn.

Conclusion

In view of the above amendments and remarks, it is believed that this application is now in condition for allowance, and a Notice thereof is respectfully requested.

Applicants' undersigned attorney may be reached at 416-307-4161. All correspondence should continue to be directed to our address given below.

Respectfully submitted,

Attorney for Applicants

Registration No. 57777

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Advisory Action Before the Filing of an Appeal Brief	Application No. 10/046,542	Applicant(s) JEFFERIES ET AL.	
	Examiner Anne Marie S. Wehbe	Art Unit 1633	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 27 September 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☒ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☒ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: *see attached*. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☒ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,3, 7-8, 14, and 17-30*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

Attachment to Advisory Action

3. cont. Applicant's claim amendment proposed the cancellation of claims 1-20, 22-24, 27, and 29-30, the amendment of claims 21, 25-26, and 28, and the addition of new claim 31. However, proposed claim 21 as amended and new claim 31 recite that the methods are practiced in an "organism". The previously pending claims under examination were directed to the practice of the methods in "animals". The terms "organism" and "animal" are not equivalent and the practice of the instant methods in any "organism" including bacteria and yeast would require additional consideration.

11. cont. As noted above, the claim amendment has not been entered and therefore applicant's arguments concerning the rejections of the claims under 35 U.S.C. 112, first paragraph, and 35 U.S.C. 102, and the obviousness type double patenting rejection are moot. Please note, however, that the proposed claim amendment would have overcome the 112, first, and 102 rejections had the claims been limited to "animal". In the interest of compact prosecution, it is further noted that had the proposed claim amendment been entered, the amendment would NOT have overcome the obviousness type double patenting rejection. The instant claims and the claims of the '770 patent are not patentably distinct for reasons of record. This rejection can be overcome by applicant's submission of a terminal disclaimer.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Dave Nguyen, can be reached at (571) 272-0731. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

'NE M. WEHBE' PH.D
'ARY EXAMINEE

Atty Dkt: 50500-963

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	:	Examiner: Anne Marie Sabrina Wehbe
JEFFRIES, William Arthur et al.	)	
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Application No.: 10/046,542	)	
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Filed: January 16, 2002	)	
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For: METHOD OF ENHANCING AN IMMUNE RESPONSE	)	
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Alexandria, VA 22313-1450

RESPONSE TO FINAL ACTION

Sir:

The present letter is filed in response to the Final Office Action dated June 27, 2006.

In response to the June 27, 2006 Final Office Action, please enter the following amendments and remarks.

Amendments to the Claims are reflected in the listing of claims which begins on page 3 of this paper.

Remarks begin on page 5 of this paper.

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1.-20. (Cancelled)

21. (Amended) A method of enhancing ~~an immune~~ a cytotoxic T-lymphocyte response in an organism to ~~a~~ tumor ~~antigen~~ cells which express low to non-detectable levels of peptide/MHC class 1 complexes on the cell surface, comprising:

administering ~~an effective amount of an agent that can augment the level of a TAP-1 molecule in a target cell bearing the tumor antigen to a cell or animal in need thereof,~~

~~wherein the agent is a vector comprising~~ *ex vivo* a nucleic acid sequence encoding ~~the~~ a TAP-1 molecule into said tumor cells;

irradiating said tumor cells; and

introducing said tumor cells containing TAP-1 nucleic acid sequences into said organism.

~~wherein the vector is capable of transforming the target cell so that the expression of TAP-1 is increased and the immune response to the tumor antigen is enhanced.~~

22-24. (Cancelled)

25. (Amended) The method according to claim 21, wherein the ~~animal~~ organism is also subjected to surgery, radiation, chemotherapy, immunotherapy or photodynamic therapy.

26. (Amended) The method according to claim 21, wherein ~~the agent is administered~~ said introducing step is performed intraperitoneally, intratumorally, subcutaneously, intravenously, orally, mucosally, submucosally or intradermally.

27. (Cancelled)

28. (Previously presented) The method according to claim ~~27~~ 31 wherein the viral vector is selected from the group consisting of vaccinia based vectors, adenovirus based vectors, lenti virus based vectors and HSV based vectors.

29-30. (Cancelled)

31. (New) A method of enhancing a cytotoxic T-lymphocyte response in an organism to tumor cells which express low to non-detectable levels of peptide/MHC class 1 complexes on the cell surface, comprising:

introducing into the organism, at a location into or near the tumor cell a viral vector encoding a TAP-1 molecule into in a manner which causes uptake by said tumor cells of said viral vector, resulting in the expression of TAP-1 in said tumor cells.

32. (New) The method according to claim 21, wherein said nucleic acid sequence encodes both the TAP-1 molecule and a TAP-2 molecule.

33. (New) The method according to claim 31, wherein said viral vector encodes both the TAP-1 molecule and a TAP-2 molecule.

34. (New) A method of enhancing a cytotoxic T-lymphocyte response in an organism to tumor cells which express low to non-detectable levels of peptide/MHC class 1 complexes on the cell surface, comprising:

introducing into the organism, at a location into or near the tumor cell a plasmid vector encoding a TAP-1 molecule into in a manner which causes uptake by said tumor cells of said plasmid vector, resulting in the expression of TAP-1 in said tumor cells.

35. (New) The method according to claim 31, wherein said plasmid vector encodes both the TAP-1 molecule and a TAP-2 molecule.

REMARKS/ARGUMENTS

By the present amendment, claims 1, 3, 7-8, 14, 17-20, 22-24, 27 and 29-30 have been cancelled, claims 21, 25-26 and 28 have been amended and new claims 31-35 have been added. Claims 21, 25-26,

28 and 31-35 are currently pending in the application. The amendments to the claims have been made without prejudice and without acquiescing to any of the Examiner's objections. Applicants reserve the right to pursue any of the deleted subject matter in a further divisional, continuation or continuation-in-part application. The amendment does not contain new matter and its entry is respectfully requested.

The Official Action dated June 27, 2006 has been carefully considered. It is believed that the following comments represent a complete response to the Examiner's rejections and place the present application in condition for allowance. Reconsideration is respectfully requested.

Double Patenting

The Examiner has indicated that claims 1, 7, 14, 17-19, 21-23 and 26-29 are rejected for obviousness-type double patenting over claims 1-10 of U.S. Patent No. 6,361,770. Of these claims, only claims 21 and 26 remain pending in the application. Applicant submits that the claims as presented herein are not covered by the claims of U.S. Patent No. 6,361,770. If the Examiner adopts the position that the claims as amended are still subject to a rejection for obviousness-type double

patenting, Applicant is willing to consider filing a terminal disclaimer.

35 USC 112, first paragraph (Enablement)

The Examiner has rejected claims 1, 3, 7-8, 14 and 17-30 under 35 USC 112, first paragraph, for lack of enablement. Applicant notes that claims 1, 3, 7-8, 14-20, 22-24, 27 and 29-30 have been cancelled. In response to the rejection over the remaining claims, Applicant submits the following remarks.

Examiner's remarks

The Examiner has identified the following scope of enablement (at Page 4 of the Final Action): 1) methods of augmenting a CTL response in a mammal to tumor cells expressing a low or nondetectable level of peptide/MHC class 1 complexes on the cell surface comprising ex-vivo introduction of a nucleic acid encoding TAP-1 into the tumor cells followed by introduction of the tumor cell into the mammal and 2) methods of augmenting a CTL response in a mammal to tumor cells expressing a low or nondetectable level of peptide/MHC class 1 complexes on the cell surface comprising introducing a viral vector encoding TAP-1 into or near the tumor cell. This scope of enablement is considered non-exhaustive, as both the Examiner and Applicant have identified other methods enabled by the disclosure.

In response, Applicant has amended claim 21 and added new claims 31 and 34 to reflect the scope of enablement described by the Examiner. Dependent claims have been cancelled or modified accordingly to reflect the amended and new claims. In particular, all claims directed to methods of enhancing an immune response to a viral antigen have been cancelled.

In light of the above, Applicant submits that the pending claims are fully supported by the application.

In light of the above, Applicant respectfully requests that the rejection to the claims, pursuant to 35 U.S.C. 112, first paragraph, for lack of enablement, be withdrawn.

35 U.S.C. 102 rejections

Spies et al. (1992)

The Examiner has rejected claims 1, 3, 7-8 and 19 under 35 U.S.C. 102(b) as being anticipated by Spies et al. (1992) Nature, Vol. 355, 644-646. As the claims in question have all been cancelled, Applicant respectfully submits that this rejection be withdrawn.

Powis et al. (1991)

The Examiner has rejected claims 1, 3, 7-8 and 19 under 35 U.S.C. 102(b) as being anticipated by Powis et al. (1992) Nature, Vol. 354, 528-531. As the claims in question have all been cancelled, Applicant respectfully submits that this rejection be withdrawn.

Conclusion

In view of the above amendments and remarks, it is believed that this application is now in condition for allowance, and a Notice thereof is respectfully requested.

Applicants' undersigned attorney may be reached at 416-307-4161. All correspondence should continue to be directed to our address given below.

Respectfully submitted,

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